

CASE

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A Young Adult with Myoclonic Seizure

A 21-year-old man was referred to dermatology clinic for skin biopsy. He presented to neurology center with behavioral changes with cognition and memory disorders. He had two episodes of generalized tonic clonic seizure and series of myoclonic jerks in his limbs and face especially after awakening since several months ago. In neurological examination, he had mini mental score as 13; with some degree of bradykinesia, limb rigidity and dysarthria. He had leaved school because of inability to learning. His sister had died 5 months ago from the same disease.

We performed biopsy from his right axillary skin. Histopathological examination revealed multiple intracytoplasmic homogenous pale basophilic globi in apocrine glands acini which were showing PAS positive reactivity in special staining. Remainder of epidermis and mid reticular dermis was unremarkable (Figures 1 and 2).

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What is your diagnosis?

Move on to next page for the answer and discussion.

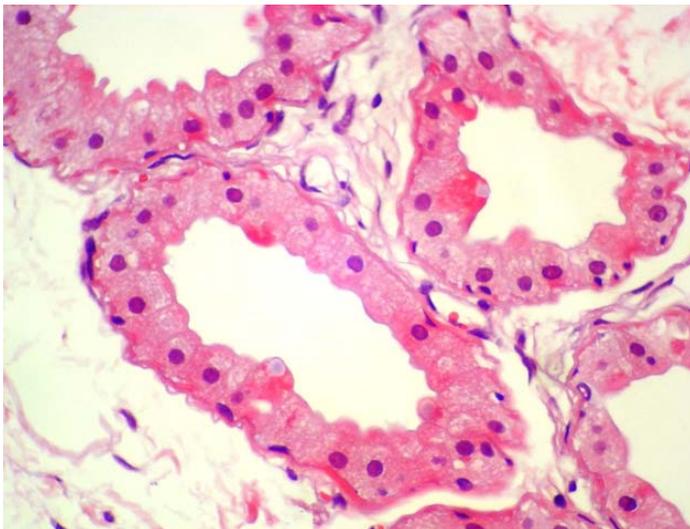


Figure 1. Intracytoplasmic homogenous pale basophilic globi (Lafora bodies) in apocrine glands acini. (H&E *40)

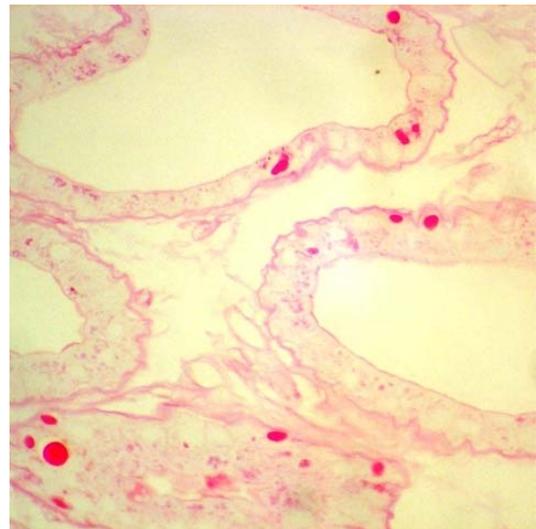


Figure 2. Large, purplish-red granules in the outer layer of eccrine duct cells. (PAS *40)

Diagnosis: Lafora Disease

Discussion

Lafora disease is a familial, degenerative disorder with the clinical triad of seizures, myoclonus and dementia. This metabolic disorder is transmitted by autosomal recessive inheritance. The onset of disease is in late childhood and adolescence (between 10 and 18 years) with generalized tonic-clonic seizures. Ultimately, myoclonic jerks appear; these are accompanied by visual seizures and cognitive decline and become more apparent and constant with progression of the disease. Mental deterioration is a characteristic feature and becomes evident within one year of the onset of seizures. Death occurs 2-10 years after onset of symptoms^{1,2}.

Cutaneous lesions are rarely present. Neurologic abnormalities, particularly cerebellar and extrapyramidal signs are prominent findings. The EEG shows polyspike-wave discharges, particularly in the occipital region, with progressive slowing and a disorganized background^{1,2}.

A characteristic feature is the widespread formation of poorly branched, water-insoluble glycogen-like polymers (polyglucosan) known as "Lafora bodies", which accumulate in the cytoplasm of neurons, skeletal muscle, liver and other tissues³. They were first described by Lafora, who considered them to consist of amyloid. They are PAS positive and diastase resistant inclusions, well seen in the excretory ducts of eccrine and apocrine sweat glands of clinically normal skin⁴⁻⁷. Electron microscopy shows that these inclusions are round or oval, non-membrane bound and often juxtanuclear in position⁶. They are composed of fine filamentous material, dark-staining granules and vacuoles¹.

Diagnosis may be established by examination of a skin biopsy specimen for these inclusions. The number of inclusions may vary with the biopsy site¹; axillary skin is favored⁵. Detection of Lafora bodies in skin biopsy specimens has been the traditional method of making the diagnosis; however, genetic testing is now available for known defects and perhaps is more sensitive⁸.

The gene responsible maps to chromosome 6q23-25⁵. A mutation in the EPM2A gene, encoding Laforin, a tyrosine kinase inhibitor, is responsible for 80% of the cases of Lafora-type progressive myoclonic epilepsies. Laforin may play a role in the regulation of normally structured glycogen metabolism that functions to suppress excessive glycogen phosphorylation³. Other gene loci also have been associated with Lafora's disease, including NHLRC1 (formerly EPM2B) in the 6p22 region⁹.

Treatment is largely supportive with conventional antiepileptic and antimyoclonic drugs. The myoclonic jerks are difficult to control, but a combination of valproic acid and a benzodiazepine (clonazepam) is effective in controlling the generalized seizures⁹.

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